

58 Nov 7401510 27 FEB 1998

We claim:

1. An isolated polynucleotide selected from the group consisting of:
 - (a) a polynucleotide encoding the polypeptide comprising the amino acid sequence of SEQ ID NO:1;
 - (b) a polynucleotide encoding the polypeptide comprising the amino acid sequence of SEQ ID NO:2;
 - (c) a polynucleotide capable of hybridizing to and which is at least 95% homologous to the polynucleotide of (a) or (b).
2. The polynucleotide of claim 1 comprising the sequence of the group consisting of the second line of Figure 5 and SEQ ID NO:3.
3. The polynucleotide of claim 1 comprising the sequence of the group consisting of the third line of Figure 5 and SEQ ID NO:4.
4. An isolated polynucleotide selected from the group consisting of:
 - (a) a polynucleotide encoding a polypeptide comprising the sequence of SEQ ID NO:6;
 - (b) a polynucleotide encoding a polypeptide comprising amino acids 28 to 130 of SEQ ID NO:2;
 - (c) a polynucleotide capable of hybridizing to the polynucleotide of (a);
 - (d) a polynucleotide capable of hybridizing to the polynucleotide of (b);
 - (e) a polynucleotide that is at least 95% homologous to the polynucleotide of (a); and
 - (f) a polynucleotide that is at least 95% homologous to the polynucleotide of (b).
5. An isolated polynucleotide selected from the group consisting of:
 - (a) a polynucleotide encoding a polypeptide comprising the

sequence of SEQ ID NO:7;

(b) a polynucleotide encoding a polypeptide comprising the
 sequence of SEQ ID NO:8;

(c) a polynucleotide encoding a polypeptide comprising amino acids
 5 42 to 66 of SEQ ID NO:1;

(d) a polynucleotide encoding a polypeptide comprising amino
 acids 42 to 65 of SEQ ID NO:1;

(e) a polynucleotide encoding a polypeptide comprising amino
 acids 43 to 66 of SEQ ID NO:1;

(f) a polynucleotide encoding a polypeptide comprising amino acids
 10 43 to 65 of SEQ ID NO:1; and

(g) a polynucleotide capable of hybridizing to and which is at least
 95% homologous to a polynucleotide of (a) through (f).

6. An isolated polynucleotide selected from the group
 15 consisting of:

(a) a polynucleotide encoding a polypeptide comprising the
 sequence of SEQ ID NO:9;

(b) a polynucleotide encoding a polypeptide comprising the
 sequence of SEQ ID NO:10; and

(c) a polynucleotide capable of hybridizing to and which is at least
 20 95% homologous to the polynucleotide of (a) or (b).

7. An isolated polynucleotide selected from the group
 consisting of:

(a) a polynucleotide encoding a polypeptide comprising amino acids
 25 100 to 130 of SEQ ID NO:1;

(b) a polynucleotide encoding a polypeptide comprising amino
 acids 100 to 130 of SEQ ID NO:2;

(c) a polynucleotide encoding a polypeptide comprising amino acids
 100 to 111 of SEQ ID NO:1;

(d) a polynucleotide encoding a polypeptide comprising amino
 30

RECEIVED 27 FEB 1998

- 90 -

acids 100 to 110 of SEQ ID NO:1;

(e) a polynucleotide encoding a polypeptide comprising amino acids 114 to 130 of SEQ ID NO:1; and

5 (f) a polynucleotide capable of hybridizing to and which is at least 95% homologous to a polynucleotide of (a) through (e).

8. An isolated polypeptide selected from the group consisting of the amino acid sequence of SEQ ID NO:1 and the amide thereof.

9. An isolated polypeptide selected from the group consisting of the amino acid sequence of SEQ ID NO:2 and the amide thereof.

10 10. An isolated polypeptide selected from the group consisting of a polypeptide comprising the sequence of SEQ ID NO:6, a polypeptide comprising amino acids 28 to 130 of SEQ ID NO:2, and the amides thereof.

11. An isolated polypeptide comprising the sequence of SEQ ID NO:13.

15 12. The isolated peptide of claim 11 wherein the isolated peptide is from about 28 amino acid residues to about 39 amino acid residues long.

13. An isolated polypeptide selected from the group consisting of:

20 (a) a polypeptide comprising the sequence of SEQ ID NO:7;
(b) a polypeptide comprising the sequence of SEQ ID NO:8;
(c) a polypeptide comprising amino acids 42 to 66 of SEQ ID NO:1;

(d) a polypeptide comprising amino acids 42 to 65 of SEQ ID NO:1;

25 (e) a polypeptide comprising amino acids 43 to 66 of SEQ ID NO:1;

(f) a polypeptide comprising amino acids 43 to 65 of SEQ ID NO:1;

30 (g) a polypeptide comprising at least one conservative amino acid substitution in the sequence of polypeptides (a - f); and

- 91 -

(h) the amides thereof.

14. An isolated polypeptide selected from the group consisting of:

- 5 (a) a polypeptide comprising the sequence of SEQ ID NO:9;
(b) a polypeptide comprising the sequence of SEQ ID NO:10;
and

(c) the amides thereof.

15. An isolated polypeptide selected from the group consisting of:

- 10 (a) a polypeptide comprising amino acids 100 to 130 of SEQ ID
NO:1;

(b) a polypeptide comprising amino acids 100 to 130 of SEQ ID
NO:2;

- 15 (c) a polypeptide comprising amino acids 100 to 111 of SEQ ID
NO:1;

(d) a polypeptide comprising amino acids 100 to 110 of SEQ ID
NO:1;

(e) a polypeptide comprising amino acids 114 to 130 of SEQ ID
NO:1;

- 20 (f) a polypeptide comprising at least one conservative amino acid
substitution in the sequence of polypeptides (a - e); and

(g) the amides thereof.

16. A vector comprising a polynucleotide of claim 1 operably
linked to control sequences which direct the expression of the polynucleotide.

25 17. A vector comprising a polynucleotide of claim 2 operably
linked to control sequences which direct the expression of the polynucleotide.

18. A vector comprising a polynucleotide of claim 3 operably
linked to control sequences which direct the expression of the polynucleotide.

30 19. A vector comprising a polynucleotide of claim 4 operably
linked to control sequences which direct the expression of the polynucleotide.

20. A vector comprising a polynucleotide of claim 5 operably linked to control sequences which direct the expression of the polynucleotide.

21. A vector comprising a polynucleotide of claim 6 operably linked to control sequences which direct the expression of the polynucleotide.

5 22. A vector comprising a polynucleotide of claim 7 operably linked to control sequences which direct the expression of the polynucleotide.

23. A host cell transformed with a vector of claim 16.

24. A host cell transformed with a vector of claim 17.

25. A host cell transformed with a vector of claim 18.

10 26. A host cell transformed with a vector of claim 19.

27. A host cell transformed with a vector of claim 20.

28. A host cell transformed with a vector of claim 21.

29. A host cell transformed with a vector of claim 22.

15 30. A pharmaceutical composition comprising a polypeptide of claim 8 and a pharmaceutically acceptable carrier.

31. A pharmaceutical composition comprising a polypeptide of claim 9 and a pharmaceutically acceptable carrier.

32. A pharmaceutical composition comprising a polypeptide of claim 10 and a pharmaceutically acceptable carrier.

20 33. A pharmaceutical composition comprising a polypeptide of claim 11 and a pharmaceutically acceptable carrier.

34. A pharmaceutical composition comprising a polypeptide of claim 14 and a pharmaceutically acceptable carrier.

25 35. A pharmaceutical composition comprising a polypeptide of claim 15 and a pharmaceutically acceptable carrier.

36. A method of treating a neurological disease or homeostatic dysfunction or controlling the production of a homeostatic regulatory hormone comprising introducing an effective amount of the composition of claim 18 into a mammal in need of such treatment.

30 37. An antibody that immunoreacts with an isolated mammalian

H35 protein.

38. An antibody of claim 37 which is a monoclonal antibody.
39. A kit for detecting the presence of an H35 protein in a mammalian sample comprising an antibody which immunoreacts with a
5 mammalian H35 protein or with a polypeptide of claim 10 in an amount sufficient for at least one assay and suitable packaging material.
40. A kit for detecting the presence of an H35 protein in a mammalian sample comprising an antibody which immunoreacts with a mammalian H35 protein or with a polypeptide of claim 11 in an amount sufficient
10 for at least one assay and suitable packaging material.
41. A kit for detecting the presence of an H35 protein in a mammalian sample comprising an antibody which immunoreacts with a mammalian H35 protein or with a polypeptide of claim 14 in an amount sufficient for at least one assay and suitable packaging material.
- 15 42. A kit for detecting the presence of an H35 protein in a mammalian sample comprising an antibody which immunoreacts with a mammalian H35 protein or with a polypeptide of claim 15 in an amount sufficient for at least one assay and suitable packaging material.
43. The kit of claim 39 further comprising a detecting antibody
20 which binds to the anti-H35 antibody.
44. The kit of claim 43 wherein the detecting antibody is labeled.
45. The kit of claim 44 wherein the label comprises enzymes, radioisotopes, fluorescent compounds, colloidal metals, chemiluminescent
25 compounds, phosphorescent compounds, or bioluminescent compounds.
46. A kit for detecting the presence of genes encoding an H35 protein comprising a polynucleotide of claim 1, or fragment thereof having at least 10 contiguous bases, in an amount sufficient for at least one assay, and suitable packaging material.
- 30 47. A method for detecting the presence of a nucleic acid

encoding an H35 protein in a mammalian sample, comprising the steps of:

(a) hybridizing a polynucleotide of claim 1, or fragment thereof having at least 10 contiguous bases, with the nucleic acid of the sample; and

(b) detecting the presence of the hybridization product.

5 48. A method of detecting an H35 antigen in a mammalian sample comprising the steps of:

(a) contacting the sample with an anti-H35 antibody which immunoreacts with a hypocretin polypeptide; and

(b) detecting the presence of an immunoreaction complex.

10 49. The method of claim 48 wherein said complex is detected by admixing said immunoreaction complex with a detecting antibody capable of immunoreacting with said anti-H35 antibody.

50. The method of claim 49 wherein the detecting antibody is labeled.

15 51. The method of claim 48 wherein the anti-H35 antibody is immobilized on a solid support.

52. The method of claim 48 wherein the sample comprises cells.

20 53. The method of claim 52 wherein the cells are peripheral blood mononuclear cells.

54. The method of claim 48 wherein the immunoreaction complex of step (b) is detected by flow cytometry.

55. The method of claim 48 wherein the immunoreaction complex of step (b) is detected by ELISA.

25 56. A method of claim 48 wherein the immunoreaction complex of step (b) is detected by immunoblot analysis.

57. A polynucleotide comprising the sequence of SEQ ID NO:5.

58. A vector comprising the sequence of SEQ ID NO:5.

30 59. A host cell transfected with the vector of claim 58.